

JOURNAL OF BIOENERGETICS AND BIOMEMBRANES—Volume 29, 1997

Journal of Bioenergetics and Biomembranes is an international journal devoted to the publication of original research that contributes to fundamental knowledge in the areas of bioenergetics, membranes, and transport. The subspecialties represented include membrane transport, electron transport, ATP synthesis by oxidative or photophosphorylation, muscle contraction, and biomembranes.

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Front outside cover: Are precursors translocated across the mitochondrial membranes through aqueous channels? This diagram summarizes recent electrophysiology studies that suggest that channel activities in both the inner and outer membrane may participate in mitochondrial protein import (see minireview by Jensen and Kinnally). Multi-subunit complexes of proteins in the outer membrane (TOM) and in the inner membrane (TIM) are proposed to form aqueous channels that allow passage of the precursor (shown in red) into the matrix. In this model, the outer membrane Tom20, Tom22, Tom37, and Tom70 proteins function as receptors for the cytoplasmically-synthesized precursor protein and direct the precursor into the TOM channel. The Tim44 and mt-Hsp70 proteins then "pull" the precursor through both channels into the matrix.

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Front outside cover: Fluorescence micrograph of cultured myoblasts from a patient suffering mtDNA depletion syndrome. The absence of yellow fluorescence in some cells indicates a lack of mtDNA-encoded subunit I of cytochrome *c* oxidase in these cells. (Related to the minireview by Jan-Willem Taanman.)

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Front outside cover: Schematic illustration of fixed $\alpha_3\beta_3\gamma$ subcomplex of F_1 -ATPase from thermophilic bacteria used for observation of the rotation of the γ subunit. The crystal structure of mitochondrial F_1 -ATPase is adopted to represent the thermophilic $\alpha_3\beta_3\gamma$ subcomplex. His-tag's which are supposed to fix the subcomplex to the glass plate are not shown. An actin filament is attached to the γ subunit through biotin-streptavidin-biotin. (See Invited Minireview by Yasuda *et al.*).

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Front outside cover: The cover figure provides in simplified form a current view of those genetic, biochemical, and bioenergetic events responsible for one of the most common phenotypes of many cancers, namely their propensity to catabolize glucose at high rates to help support cell growth and division. A central player is an isoform of hexokinase (Type II) which is overexpressed in many poorly differentiated cancer cells due to a combination of events involving gene amplification, a unique promoter, and mRNA stability. The overexpressed Type II hexokinase binds to the outer mitochondrial membrane where phosphorylation of glucose is facilitated by ATP generated via oxidative phosphorylation. (From the article by Mathupala, Rempel, and Pedersen.)

JOURNAL OF BIOENERGETICS AND BIOMEMBRANES

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Front outside cover: The left panel compares airway cells from a normal healthy individual with those derived from a cystic fibrosis patient following infection with *Pseudomonas aeruginosa*. After 10 hrs the medium surrounding the normal lung cells is completely free of bacteria whereas the medium surrounding CF cells contains numerous bacteria. Some have bound to the cells whereas others have entered. Mutations in the protein called CFTR (upper right panel) cause cystic fibrosis, with the deletion of phenylalanine residue F508 within the first nucleotide binding fold/domain (called NBF1 or NBD1) causing most cases (~70%). The $\Delta F508$ mutation prevents NBF1 from folding properly resulting in its retention in the endoplasmic reticulum. Failure of CFTR to traffic to the cell membrane and function as a Cl^- channel is believed to either prevent the release of antimicrobial agents contained within airway cells, or to prevent bacterial killing even though antimicrobial agents have been released. In the latter case, it is suggested that the bactericidal action of antimicrobial agents is prevented due to the higher salt content in the airways of CF patients. The lower panel shows a 3D-model of the two nucleotide binding domains of the CFTR protein, which are believed to interact, and also the position of F508. (From the article of Ko and Pedersen in this issue, and adapted from figures in references 4, 31, and 100). In addition, a few biochemical data show that the nucleotide binding domain 1 (NBF1) interacts with the cell membrane implying a dynamic and mobile nature of this domain inside the cell.

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Front outside cover: Views of a 3-D model of the voltage-gated channel of the mitochondrial outer membrane, VDAC, obtained by electron crystallography (see Minireview article by Mannella) suspended above a tomographic reconstruction of a mitochondrion (Mannella *et al.*, 1997, Trends Biochem. Sci. 22:37). Results from the Biological Microscopy and Image Reconstruction Resource of the Wadsworth Center, Albany, NY.